

AT



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,203	04/12/2001	Maurice Zauderer	1821.0020001	1700

26111 7590 04/28/2004

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER

VANDERVEGT, FRANCOIS P

ART UNIT PAPER NUMBER

1644

DATE MAILED: 04/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/833,203	Applicant(s) ZAUDERER ET AL.	
	Examiner F. Pierre VanderVegt	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-33, 35-37, 39 and 120-130 is/are pending in the application.
- 4a) Of the above claim(s) 28-30, 32, 33, 35, 37, 121-123, 125-127 and 129 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27, 31, 36, 39, 120, 124, 128 and 130 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

DETAILED ACTION

This application claims the benefit of the filing date of provisional application 60/196,472.

Claims 1-26, 34, 38 and 40-119 have been canceled.

Claims 27-33, 35-37, 39 and 120-130 are currently pending.

Election/Restrictions

1. In accordance with the original Restriction requirement and the election of September 3, 2002, **claims 28-30, 32, 33, 35, 37, 121-123, 125-127 and 129 stand as withdrawn** from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed September 3, 2002.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 27, 31, 36, 39, 120, 124, 128 and 130 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/64464 (Savage, PM; AL3 on form PTO-1449 filed March 19, 2003) in view of Cormier et al. (Int. J. Cancer 1998 75:517-524; U1 on form PTO-892), Schnell et al. (J. Immunol. 2000 164:1243-1250; V1 on form PTO-892) and Zarour et al. (AR23 on form PTO-1449 filed January 8, 2003).

It was previously stated: "Savage teaches the making and use of a compound comprising one or more Class I MHC-peptide complexes an antibody or fragment thereof specific for a cell surface marker of a tumor cell (see entire document, Figure 1 in particular), including the elected species of CEA (paragraph bridging pages 5-6 in particular) or for cell surface marker on antigen presenting cells (see

Art Unit: 1644

entire document, Figure 4 in particular. Savage teaches that the MHC molecule is linked to the carboxyl terminus of the antibody (see, for example, Figures 1 and 4 in particular).

Savage differs from the claimed invention in that the publication does not disclose class II MHC molecules or MelanA/MART (51-73) as an antigenic peptide bound to the MHC.

Cormier teaches that MelanA/MART-1 is a melanoma-associated antigen (MAA) that is present in a majority of melanomas (page 571, first column in particular). Cormier further teaches that tumor-infiltrating lymphocytes can recognize MelanA/MART-1 in the context of MHC class I presentation and can be detected in the peripheral blood of patients but "there have been few cases of objective tumor rejection" (page 571, first column in particular). Cormier also teaches that a possible explanation is that down-regulation of MAA by a tumor population provides a mechanism by which tumors escape immune recognition (page 571, second column in particular).

Schnell teaches that it is well established that T cell help can augment CTL function (Abstract in particular). Schnell further teaches that antigen presenting cells that present antigens in the context of both class I and class II stimulate a more robust cytotoxic response to the target tumor (see entire document).

The combination of references differs from the claimed invention in that they do not disclose MelanA/MART (51-73) as an antigenic peptide bound to class II MHC.

Zarour teaches that MelanA/MART (51-73) peptide was able to stimulate *in vitro* expansion of CD4+ T cells and specifically bound to MHC class II HLA-DR4 (see entire document). Zarour further teaches that CD4+ T cell reactivity against the MelanA/MART (51-73) peptide typically coexisted with a high frequency of anti-MelanA/MART (51-73) reactive CD8+ T cells in blood from HLA-A2+/DR4+ patients with melanoma (Abstract in particular).

It would have been *prima facie* obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the references. One would have been motivated with a reasonable expectation of success to create an MHC/antibody compound as taught by Savage to increase the presentation of antigenic peptides on the surface of the tumor cell. The artisan would have been further motivated to use a MelanA/MART antigenic peptide as the target because Cormier teaches that it is present in a majority of melanomas and because there may be down-regulation of MAA in tumor cells to escape immune recognition. The artisan would have been further motivated with a reasonable expectation of success to, based upon the teachings of Savage regarding the class I/antibody constructs, to also make class II/antibody constructs based upon the teachings of Schnell that T cell help (a class II driven event) augments the cytotoxic T cell response (a class I driven event) to tumors and the teachings of Zarour that no significant class I CD8+ T cell response were observed in patients in the absence of detectable class II CD4+ T cell response to MelanA/MART-1 (page 403, second column in particular)."

Applicant's arguments filed January 21, 2004 have been fully considered but they are not persuasive. Applicant contends that that combination of references do not render the claimed invention obvious because Savage does not teach or suggest substituting MHC class I complexes (claimed) for MHC class II complexes (Savage) or linking the complex with a melanoma antigen to an antibody to a colon cancer surface marker.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary

Art Unit: 1644

skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Savage teaches an MHC class I molecule linked to an antibody specific for a tumor marker to target the MHC molecule to the cancer. Savage does not teach Applicant's antigen of interest, MelanA/MART-1. However, this antigen is taught by Cormier. Cormier also teaches tumors can be rejected by T cells recognizing this antigen but such rejection of tumors is rare, possibly due to down-regulation of expression of MelanA/MART-1 by the tumors in order to evade detection by those T cells. Accordingly, the artisan would recognize that boosting the antigenic presence on those cells would increase the likelihood of detection by the T cells. As correctly pointed out by Applicant, these teachings only specifically address MHC class I T cells. However, Schnell teaches that stimulating MHC class II helper T cells would enhance the MHC class I cytotoxic response because presenting antigens in the context of both MHC class I AND MHC class II results in an enhanced cytotoxic response to the antigen. Zarour teaches that the 51-73 peptide of MelanA/MART-1 can stimulate expansion of MHC class II-restricted helper T cells. The Court has stated that both the suggestion and the expectation of success must be **founded** in the prior art (emphasis added; *In re Dow Chemical*, 5 USPQ2d 1529 (Fed. Cir. 1988)). The term "founded" refers to a foundation, meaning not only what is explicitly stated in the references, but also what would be in the knowledge base of the practitioner of the art. In the present case, the artisan would have recognized that the teachings of Savage could be used to increase the presence of antigen on tumor cells to overcome the protective mechanism taught by Cormier. Further, the artisan would have recognized from the teachings of Schnell that stimulation of helper T cells to react to the same cells as cytotoxic cells would enhance that cytotoxic response and would have recognized from the teachings of Zarour that the MelanA/MART-1 51-73 peptide can be used to stimulate helper T cells in the context of MHC class II. Applicant points out that the Court has said in *In re Vaeck* (20 USPQ2d 1438 (Fed. Cir. 1991)) that the teaching or suggestion to modify the prior art must come from the prior art itself, and not the application. The Examiner points out further that in the same decision the Court also said that the expectation of success in light of the prior art need only be a reasonable one and not absolute predictability. Given the level of skill attributable to the person of ordinary skill in the art at the time the invention was made, the artisan would have understood that engineering MHC class II molecules to bind to the same cancer cells as MHC class I and provide support for the cytotoxic response (Savage) would have provided a reasonable expectation that the normally low response to MelanA/MART-1 (Cormier), generating a more robust response (Schnell) to the same antigen (Zarour). References can be combined not only for what they individually suggest but also

Art Unit: 1644

for what they, taken as a whole, would suggest to the person having ordinary skill in the art at the time the invention was made. See *In re McLaughlin*, 170 USPQ 209 (CCPA 1971).

Conclusion

3. No claim is allowed.


4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

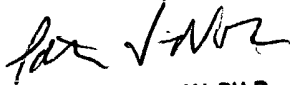
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. 
Patent Examiner
April 22, 2004


PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER

4/27/04